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Case Report

A rare case of McCune Albright syndrome

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ABSTRACT

McCune Albright syndrome is characterized by the clinical triad of precocious puberty, polyostotic fibrous dysplasia, and café-au-lait pigmentation. Authors reported the case of a 6 years old girl presenting with vaginal bleeding. Investigations showed high serum oestrogen levels, with low FSH and LH levels. Ultrasonography revealed a multiloculated right ovarian cyst. Based on the history and investigations, the patient was diagnosed as a case of precocious puberty. In order to rule out the presence of any ovarian malignancy, tumour markers were sent and found to be within the normal range. A CT pelvis was done which revealed fibrous dysplasia of the pelvic bone. The coexistence of precocious puberty with fibrous dysplasia confirmed the diagnosis of McCune Albright syndrome.

Keywords: McCune Albright, Precocious puberty

INTRODUCTION

McCune Albright syndrome (MAS) is a rare genetic disorder that occurs due to the mutation in the guanine-nucleotide binding protein alpha-subunit (GNAS1) gene. Its prevalence is estimated to range between 1/100 000 and 1/1 000 000.^{1,2} This mutation of GNAS gene is a post-zygotic event, which leads to a mosaic presentation of the gene. This explains the broad clinical spectrum of this disease.³ It is characterized by the clinical triad of peripheral precocious puberty, polyostotic fibrous dysplasia, and café-au-lait skin pigmentation.⁴ Many other endocrinopathies are associated with MAS, including hyperthyroidism, growth hormone excess, phosphate wasting and neonatal hypercortisolism.¹

Precocious puberty is the most common manifestation and if often the presenting, and only clinical sign of MAS.² It is defined as the onset of the evidence of puberty before the age of 8 years. This includes the presence of either of the following: development of breasts (thelarche), appearance of pubic hair (pubarche),

and beginning of menstruation (menarche). Epiphyseal closure can also occur earlier, thus leading to short stature of those affected by precocious puberty. Mental development can be either retarded or advanced. Later on, reproductive life is normal, and menopause also occurs normally.⁵ Precocious puberty can be either GnRH dependent (central) or GnRH-independent (peripheral). MAS is a type of peripheral precocious puberty, which is GnRH independent being caused by the peripheral secretion of sex steroids.⁵ In girls with precocious puberty, oestrogen levels are elevated, whereas serum LH and FSH levels are low. Even bone age determinants show advanced aging which explains the presence of fibrous dysplasia and fractures.⁶ Precocious puberty occurs in almost 85% of cases of MAS and is often the complaint patient presents with.¹

Fibrous dysplasia (FD) is a genetic skeletal disorder in which normal bone is replaced by abnormal bone structure in the dysplastic FD lesions.³ Fibrous dysplasia most commonly involves the proximal femur and skull base. Ninety percent of the disease burden is established

by 15 years of age, and the incidence of fractures is greatest in childhood, around 6 to 10 years.⁷

Café-au-lait spots, which are yellow-brown pigmentation of the skin, are most commonly found on the trunk, nape of neck, and buttocks. It has a typical appearance in MAS, known as the coast of Maine due to its jagged borders.^{5,7}

CASE REPORT

The patient, a 6 years old girl, reported to the gynaecology outpatient department of JK Hospital, Bhopal with chief complaint of bleeding per vaginum since 2 days. She had a normal developmental history, and no previously existing medical condition. On examination, there was presence of Tanner stage 3 thelarche, corresponding to enlargement of breast and areola with no separation of contour. There was however an absence of pubic and axillary hairs. Per abdomen examination was soft and non tender. On local examination, no obvious signs of assault were seen. The patient's clothes were mildly blood stained.

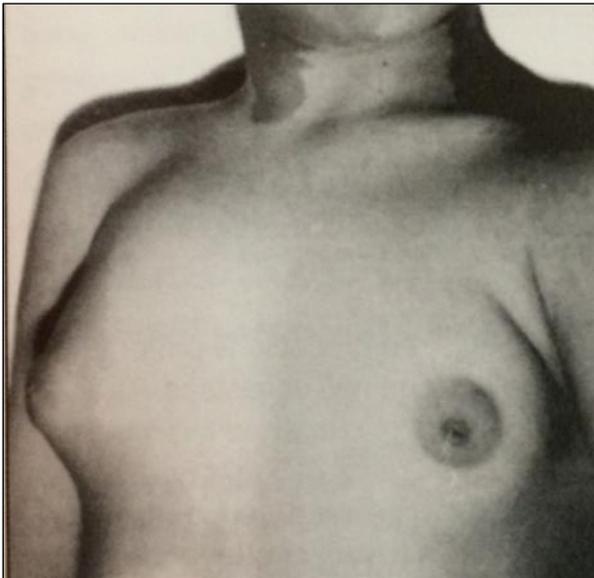


Figure 1: Precocious puberty seen as part of MAS in a young girl with well-developed breasts.⁵

A complete hormonal assay and ultrasonography imaging was advised. The patient's serum estradiol was 267.8pg/ml, higher than normal. Serum follicular stimulating hormone (FSH) and luteinizing hormone (LH) levels were < 0.30 and < 0.07 respectively, lower than the normal range seen during menstruation. Ultrasonography revealed a multiloculated right ovarian cyst. Based on the history and investigations, the patient was diagnosed as a case of peripheral precocious puberty. However, in order to rule out the presence of any ovarian malignancy, further tests were advised. All tumour markers, including alpha feto-protein, LDH, beta hCG and CA 125, were found to be within the normal range. A

CT pelvis was done which revealed not only the presence of the ovarian cyst, but also of fibrous dysplasia of the pelvic bone. Following this, multiple x-rays of long bones were taken which showed the presence of polyostotic fibrous dysplasia. The coexistence of precocious puberty with fibrous dysplasia therefore made the diagnosis of MAS.

Once the diagnosis was made, further management and treatment was aimed at blocking the aromatization and estrogen production. For this, aromatase inhibitor letrozole 2.5 mg once daily was prescribed.

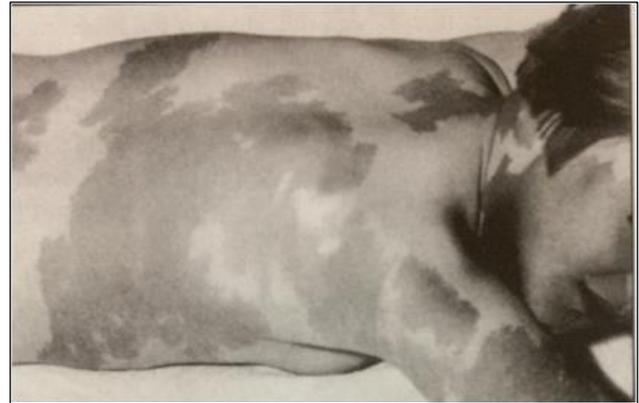


Figure 2: Patchy yellow-brown pigmentation seen in a young girl with MAS.⁵

DISCUSSION

In order to reach the diagnosis of MAS, it is not necessary to have all three of the following symptoms: precocious puberty, fibrous dysplasia and café-au-lait pigmentation. Atypical or incomplete forms of the syndrome can also occur, with only one or two of the above symptoms present, as seen in this case report.⁸ Patient can also present with various other endocrinopathies. Due to the broad clinical spectrum, and varied presentations, it often becomes difficult to form a diagnosis.

Investigations are essential to confirm the diagnosis of MAS. Hormonal study has to be done first and foremost. Then, imaging is necessary and can include X-ray, CT scan and MRI of the skeletal system. It is important to rule out the presence of any malignancy as precocious puberty can be seen in oestrogen-producing tumours such as granulosa and theca cell tumours.⁴ Biopsy shows the characteristic feature of fibrous dysplasia of bone where there is absence of the lamellation pattern seen in normal bone under polarized light. Further, genetic testing can be done. However, due to the mosaic nature of the gene, negative results can be found that do not exclude the presence of mutation.⁷

It has been a challenge until now to establish a safe and effective long term treatment for precocious puberty in girls with MAS. Drugs, such as aromatase inhibitors, that

block the biosynthesis of oestrogens have been used in the treatment of MAS.⁹ The rate-limiting step in the conversion of testosterone to estradiol and androstenedione to estrone is catalyzed by aromatase, and therefore by binding to cytochrome p450 of aromatase, aromatase inhibitors will interfere with this step and lower the levels of circulating oestrogen.¹⁰ Study conducted by Xi Wang and Qi Yu in which the study participants were treated with letrozole showed that it was highly effective at decreasing the rate of skeletal maturation, thus improving the bone age to chronological age ratio, the growth velocity, and predicted adult height. Moreover, letrozole also showed a significant decline in vaginal bleeding.¹

This rare and interesting case was an indicator that if there is any patient presenting with precocious puberty, a diagnosis of MAS should also be kept in mind.

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